SYPHILIS OF THE LIVER

ROBERT P. A. MACAULAY,
M.B., Ch.B.

A THESIS PRESENTED TO THE FACULTY OF THE UNIVERSITY OF EDINBURGH FOR THE DEGREE OF DOCTOR OF MEDICINE.

A.D. 1935.

INTRODUCTION.

Stokes[1] makes the following remark at the beginning of his chapter on Syphilis of the Liver - "Syphilis of the liver and spleen should be common. Both structures have enormous capillary sieves which strain out and dispose of large amounts of toxic and infectious circulating material with a minimum of symptomatic protest."

But he goes on to explain that "As in the nervous system, so also in the liver and spleen, there is probably a high incidence of early reaction, taking the form of congestion with enlargement of the organ, and followed by recovery as the spirochaetaemia subsides. Only a relatively small proportion of patients who, at the onset, have a visceral reaction, will have symptoms directing attention to it, and a much smaller proportion will be likely to develop chronic reactions or late manifestations," while on the other hand Hazen[2] contents himself with the dictum that the liver is sometimes affected in secondary syphilis and even more commonly in tertiary lues. In striking contrast with this Lloyd Thompson[3] asserts that involvement of the liver is the most frequent of all syphilopathies.

Some of the earliest syphilographers looked upon the liver as the chief focus of the disease. Among them was Gabrille Fallopio[4] while others held that it was only a secondary lesion. Later Jean Astruc[5] and others of his period wrote more or less completely

concerning hepatic syphilis.

John Hunter [6] merely mentions that jaundice is attributed by some to syphilis and states that if this and other diseases which are considered as due to syphilis became the cause of careful investigation it would be productive of good.

Whether this exhortation of Hunter's is widely known or not a great deal of careful investigation has been carried out and it will be my endeavour in this brief paper to collect and summarize the product of the work of the better known of these authorities and in conjunction with the cases which I report draw some conclusion which may be helpful in the diagnosis and treatment, of hepatic syphilis.

PART I

Classification of types of Hepatic Syphilis.

While most authors subdivide Syphilis of the liver into the two stages of the disease early, and late it is my opinion that the classification given by Stokes[7] is probably the best. I am therefore going to adopt this classification as a working basis for the description of the condition and shall as far as possible fit my cases into it.

These are the clinical types as used by Stokes

1. Early acute benign Hepatitis.
2. Syphilitic Destructive Hepatitis or Acute Yellow Atrophy.
3. Mild Chronic Hepatitis of Latency.
4. Diffuse and localised Gummatous Hepatitis.
5. Perihepatitis
6. Chronic and (interstiteal) Pericellular cirrhosis of Heredo syphilis.

Although these are enumerated as separate entities it must be realised that they may be related, Thus Acute Yellow Atrophy may supervene on Early Acute benign Hepatitis and similarly Perihepatitis is usually caused by an extension of syphilis of the Parenchyma of the liver to the adjacent portion of the peritoneum covering it.

1. Early Acute Benign Hepatitis.

Gubler[8] in 1853 first called attention to the association of jaundice with secondary syphilis in a memoir in which he reported five cases.

Since then cases have been reported by Werner[9] Lancereaux[10] Lasch[11] and others. It is, however, to Rolleston[12] and Osler[13] that we owe the best descriptions of this condition and it is from their monographs that the following description is largely compiled.

It is a rare condition almost certainly occurring in less than one per cent of all cases showing marked secondary manifestations. Werner, in his article mentioned above, states its frequency as 0.37 per cent. Little is known of the pathology of this condition but there are a number of theories as to its cause; first a syphilitic catarrhal cholangitis, second due to a condyloma of the bile duct, third pressure exerted by enlarged lymphatic glands on the portal fissure.

The most rational theory seems to be the one of Rolleston who believes it to be a catarrhal condition, of the small intra-hepatic bile ducts, which is merely part of a general syphilitic hepatitis. There is probably a pericellular infiltration of lymphocytes as seen in congenital syphilis.

There is no proof that jaundice is due to mercury in as much as it is usually cured by the administration of this drug. The arsenical drugs may cause jaundice but the condition often occurs in untreated cases and the drug may be given with good results to cases of Benign Hepatitis.

The condition occurs about as frequently in men as in women, it usually comes on suddenly and coincides with the arrival of the secondary rash. Thompson[14] states that it may appear slightly later but usually within six months following the chancre.

The jaundice may be slight or well marked when it tends to become chronic unless there be antisyphilitic

treatment. It is usually accompanied by slight gastric symptoms such as a sense of fulness in the epigastrium and eructations.

The liver is more or less enlarged and tender and the spleen may be palpable.

The stools may or may not be clay coloured depending on the severity of the process.

Diagnosis.

The only condition which could be mistaken for Benign Hepatitis is Acute Catarrhal Jaundice. In the latter condition the onset is more acute and the symptoms much more pronounced.

The presence of the typical secondary rash and of a recently healed chancre would suggest a Wassermann Reaction, if this had not already been performed, which would be positive. The prognosis is good as a rule although in some rare cases acute Yellow Atrophy may supervene. This may result in the untreated or inadequately treated cases or in the case which is given too much arsenic.

Treatment.

The rational treatment seems to be laid down by Stokes [15] who says:-

Inasmuch as this condition is a complication of early syphilis, in which for the sake of securing abortive cures, the inclination is to press the arsenical treatment as much as possible, a caution should be given against the use of methods which tax the liver heavily. While they may be tolerated

by some, it is to be expected that others will be precipitated into a severe Herxheimer reaction or a toxic hepatitis.

On the other hand smaller doses of neo-arsphenamin (neo-salvarsan) 0.3 to 0.4 gms., are usually well borne for the first three or four injections and accomplish the necessary superficial sterilization of the patient's infectious lesions, after which intensive treatment with mercury and larger doses of salvafsan should be resumed and persisted in. Iodide is not necessary in cases of benign early hepatitis since there is little granulomatous change.

Syphilitic Destructive Hepatitis.

This is a somewhat rare but important complication of syphilis. In 1908 Fischer[16] collected fifty definite cases and since that time others have been reported.

This condition is described as being associated with the early period of Syphilitic infection at times even preceeding the secondary eruption as in the case of acute syphilitic nephritis.

It may start as a destructive hepatitis or may come on without warning on top of the benign form of icterus. Thompson[17] goes so far as to say that it almost always follows the milder type.

If this is the case, and Stokes[18] says that the incidence of the grave icterus is 10 per cent in cases of benign hepatitis, the rarity of the disease is evident.

However rare it is the condition must be considered and excluded in every case of acute yellow atrophy.

It must be stated that there are no particular features which serve to distinguish these cases from those of the ordinary type of acute yellow atrophy.

Acute Yellow atrophy whatever its aetiology is essentially a rapid autolysis of liver substance. It has been demonstrated by Truffi[19] that both mercury and arsenical preparations can cause autolysis of the liver, and Tileson[20] has quoted a case where mercurial inunctions in a non-syphilitic were followed by the development of acute yellow

atrophy. While it is possible in some instances that this complication may be caused by treatment, it occurs with as great frequency in the untreated cases.

Some authors especially the French headed by Milian [21] hold that the condition is not so much the result of the primary or original infection, as of a fulminating relapse following inadequate treatment similar in its causal mechanism to the types of meningeal relapse which produce the familiar neuro-recurrence.

Most syphilologists do not subscribe to that view but believe that the grave icterus is a syphilotoxic phenomenon giving rise to a destruction of liver cells and a jaundice of non-obstructive type.

Harrison [22] states that this condition is commoner in women than in men and may be associated with pregnancy.

It is to Wile [23] and Karshner that we owe the most complete description of the symptoms of the acute yellow atrophy of the liver of syphilitic origin.

The condition has an insidious onset with mild but steadily deepening jaundice. There is malaise anorexia, and vomiting and this may or may not be accompanied by fever. The patient complains of muscular aching and at times of severe abdominal cramps. A toxic condition then supervenes with emaciation and the typhoid state. The liver

enlarges at first and may do so to a considerable extent but as the toxic condition advances the liver rapidly diminishes in size. Ascites may appear early but usually comes on when the liver shrinks. Haemorrhages from the bowel, haematemesis, purpura of the skin and petechial haemorrhages from gums and buccal mucosae are not uncommon.

As the intoxication becomes more intense Psychosis with delirium, violent headaches and at times maniacal symptoms develop or there may be insomnia with depression. Apart from the deep jaundice the late symptoms suggest those of meningitis or uraemia with which latter condition those cases accompanied by severe nephritis are undoubtedly complicated.

Wile stressed the obstinacy of constipation in this condition and a peculiarly offensive stool.

Laboratory aids to the diagnosis of acute yellow atrophy may be found in the presence of leucin and tyrosine crystals in the urine of most cases although this is not an invariable rule as Stokes [24] did not find it in the case reported by him. Tests for hepatic function show a rapid decline but this is of no diagnostic help, as it occurs in all progressive changes. A rising blood area is of unfavourable prognostic significance as it is probably the result of renal failure quite as much as of liver inefficeincy.

Diagnosis

As stated above there are no features of this condition which distinguish it from other types of

acute yellow atrophy. The diagnosis must therefore be based on the diagnosis of syphilis taking into account the stage of the disease at which this complication usually occurs.

Accordingly we would look for a primary sore or a recent scar of one, the presence of a secondary rash and the finding of a positive Wassermann Reaction. The diagnosis would be made easier if the grave icterus supervened on a benign hepatitis. I think it can be said that the syphilitic aetiology would be proved beyond doubt if the case responded to antisyphilitic treatment.

Treatment.

The condition is a very serious one and when the diagnosis is arrived at heroic measures are indicated

Although some authorities are inclined to spare the liver from the effects of arsenic. Stokes[25] holds that in therapeutic doses arsenic does not seriously impair hepatic function, and therefore both arsenic and mercury may be employed in cases in which the outcome is grave.

Hazen[26] suggests that as some cases of necrosis of the liver may be due to mercury or arsenic cognisance must be taken of the drug which is being employed when the complication arises. Thus if the patient is receiving arsenic when he develops grave icterus it should be stopped and the treatment continued with mercury and vice versa.

If however, the patient has been getting no

antisyphilitic medication he advocates the administration of small doses of neo-salvarsan every two or three days. Wile[27] reports a case which responded to calomel intramuscularly, and iodid by mouth.

The Mild Chronic Hepatitis of Latency.

This condition is usually quite asymptomatic and is often overlooked in Physical examination or discounted as of no significance. It is quite possible that the condition may even disappear without attracting attention.

Stokes [28] found in a series of 419 cases, in which recognised syphilitic hepatitis had been excluded of 40 who had enlarged livers 33 had positive blood Wassermann reactions. Of 20 patients with both Hepatic and Splenic enlargement 17 had positive blood Wassermann reactions.

These striking facts show how easily the "Latent Liver" is missed unless looked for by the alert observer. Conversely it is a warning that the "Latent liver," and spleen should be an indication to do a Wassermann Reaction and a valuable aid in the diagnosis of syphilis in the later stages of the disease.

The most common sign or symptoms are ascites and pain. The ascites usually comes on much later than in other forms of cirrhosis. The pain is more or less severe and radiates to the right shoulder.

The finding of an enlarged liver without symptoms should be a warning to look for signs of syphilis. As this is a late manifestation a careful history of exposure, the presence of a past ulcer and of transient rashes should be gone into.

The Wassermann reaction should be performed but in this condition it may give variable results. If it

is negative it should be done repeatedly and checked by using another test such as the Sachs Georgi or Kolmer.

The lines of treatment of this condition will be considered along with those of the other late types of hepatic syphilis.

Late Diffuse Hepatitis and Gummatous Hepatitis.

It would be very surprising if the liver escaped the slow chronic inflammatory and degenerative changes, and fibrosis of syphilis, which are so typical of the disease in nearly every other structure of the body.

These types of cases do occur in the liver and may be present simultaneously. As Perihepatitis is usually a concomitant of Diffuse or gummatous hepatitis it can be conveniently dealt with in this section.

Again as in other types of hepatitis no true estimate of the occurrence of these types may be made and apart from stating that they are by far the commonest syphilitic affections of the liver some estimate of their frequency may be surmised from the following figures.

Osler [29] states that, in 18 years at the John Hopkin's Hospital only 30 cases were diagnosed during life and only 40 cases were recognised at autopsy.

Flexner [30] reporting 5088 necropsies found 88 cases of hepatic syphilis. It must be borne in mind that these figures were before the days of the Wassermann Reaction and before syphilis was recognised

to be as prevalent as it is today hence many cases have undoubtedly escaped discovery.

A later estimate was made by Symmers[31] who reported 314 autopsies upon syphilitic subjects and found syphilis of the liver 105 times.

The pathology of these conditions in the liver is the same as in other organs it seems unnecessary to deal with a subject which is so well known.

The clinical picture of the cases varies as to the proportion that interstitial fibrosis bears to localised gumma. The signs and symptoms depend on the location of the fibrosis or gummatous lesions with respect to the important structures of the liver and on the progress of the disease.

Rolleston[32] states that for convenience the clinical manifestations of late hepatic syphilis may be grouped under the following heads:

1. Where symptoms suggest portal cirrhosis or simple chronic peritonitis or perihepatitis.
2. Presenting the features of widespread amyloid disease.
3. Suggesting tumour of the liver, such as malignant growth, hydatid or enlarged Gall Bladder.
4. Imitating suppuration of the liver.
5. Resembling choletithiasis
6. Resembling chronic splenic anaemia.
7. Where the clinical features resemble hypertrophic biliary cirrhosis.

I. Cases imitating cirrhosis. These cases are

far the commonest and there are many reported cases in the literature. It is probable that the reports of cured cases of cirrhosis of the liver are based upon syphilitic lesions in many cases.

Usually there is a serous ascites but this may be either chyliform or even haemorrhagic. Harrison[33] writes that in diffuse interstitial hepatitis ascites is usually a prominent feature which may be early or not appear until comparatively late. A point of some diagnostic importance is that unlike the ascites of other liver diseases it may disappear and recur.

As a rule other signs of portal obstruction are less marked than in true cirrhosis but haemorrhoids occur and attacks of haematemisis are recorded. Jaundice is rare. The ascites is probably produced by pressure on the portal vein but in some instances by a local peritonitis due to a superficial gumma.

At first the liver is enlarged but as contraction takes place due to scar tissue replacing gummata the liver becomes smaller.

It is highly probable that many cases of atrophic cirrhosis are due to syphilis, in fact Symmers[34] says that in about 80 per cent of all cases diagnosed as atrophic cirrhosis the Wassermann Reaction was positive.

II. Rolleston states that at times there may be a gumma in the liver associated with amyloid degeneration. The presence of an enlarged spleen and of a marked Albuminuria would make one suspect the more serious condition.

III. Solitary or multiple large gummata not infrequently imitate malignant nodules in the liver and it is highly probable that many a patient has not had the proper treatment because malignancy was diagnosed. However there are certain points of difference, which help to throw light on the diagnosis.

Gummata are usually situated upon the anterior surface of the liver so that the tumour masses are more easily defined than in carcinoma which is apt to start deep in the liver substance.

Then too cancer nodules usually grow steadily and more rapidly than gummata which reach a certain point and begin to contract.

Gummata are usually found in younger subjects and the presence of an enlarged spleen and albuminuria point to syphilis.

In carcinoma pain and cachexia are prominent.

While the presence of other syphilitic manifestations, and a positive Wassermann reaction help in the diagnosis it must be remembered that the syphilitic may develop carcinoma and the final test in these cases is the rapid response to antisyphilitic treatment.

IV. Cases with fever, resembling hepatic suppuration have been discussed rather fully by Edwards.[35] The pyrexia in these cases is due either to breaking down gummata, a rapid extension of the syphilitic process in the liver or the involvement of the peritoneum. The fever may suggest hepatic abscess,

malaria, tuberculosis or even typhoid fever. Whichever of these is simulated must be excluded by the many means at our disposal such as the history in hepatic abscess and malaria, the careful examination for a tubercular lesion and cutaneous test and agglutination tests, and cultures in typhoid. The most difficult to exclude is sepsis for in the fever associated with syphilitic hepatitis the temperature and pulse may fluctuate, and the leucocyte count may be raised and the Arneth count suggest sepsis. A case of gummata of the liver reported by Osler[35] had such a high leucocyte count as to suggest leucaemia. Secondary infection may of course, take place in a gumma so that a primary abscess is closely simulated.

The therapeutic test is the great stand by as the fever in syphilis is almost invariably ameliorated quickly by treatment.

V. Cases of syphilis of the liver resembling gall stones have been studied by Riedel[36] and others. Jaundice is not common in hepatic syphilis but occasionally the pressure of a gumma or the drag of scar tissue upon the portal fissure may lead to this phenomenon.

In rare cases this jaundice may be accompanied by colicky pains that suggest gall stones.

Stokes[37] reports such a case - a physician, who had an accidental infection of the finger, demonstrated the syphilitic gall-bladder syndrome. His Wassermann reaction was persistently negative but on the

strength of a positive Kolmer reaction he was given antisyphilitic treatment with complete success all his symptoms clearing up. Occasionally a gumma may simulate a distended gall bladder as in the case reported by Parker [38]

The differential diagnosis may be very difficult and X-ray should be taken after ST.I.P.P. or some other opaque substance has been administered.

It is a good dictum that all patients with the gall bladder syndrome who have a positive Wassermann Reaction should have antispecific treatment to see if the condition is improved before surgery is resorted to, unless he is a critical surgical emergency.

VI. In some cases of syphilitic hepatitis the spleen may be enlarged either as a direct result of secondary syphilis as Wile [39] has shown, from amyloid changes, or from gummata, while the liver may be but little enlarged.

If an anaemia of the hypochromic type accompanies such a picture it is natural that a diagnosis of splenic anaemia may be made as in the cases of Coupland [40] and Asler. [41]

Stokes [42] quotes a case where the patient symptomatically resembled Pernicious Anaemia showing sore mouth, diarrhoea and achlorhydria but where the blood picture was of the hypochromic type. This case more closely resembles Chronic Microcytic Anaemia; it was in a woman. She responded well to antisyphilitic treatment although the haemoglobin

remained a little subnormal for a long time.

The therapeutic test is the final court of appeal - all these cases simulating the blood dyscrasias.

VII. In very exceptional instances syphilis of the liver may lead to an enlarged liver with chronic jaundice and splenic enlargement as pointed out by Hanot.[43)]

As a rule the progress of the case is more rapid than in biliary cirrhosis and the spleen is not so large. There is a response to treatment in the syphilitic type.

From the above clinical classification it is obvious that late syphilis hepatitis may simulate almost any abdominal complaint. When the liver is fairly uniformly enlarged there is usually no difficulty in determining which organ is involved, but when this is not the case upper abdominal tumours have been mistaken for enlarged kidney on the right side, gall bladder at the 9th costal cartilage tumour of the transverse colon, and spleen on the left side.

Straight X-rays and Pyelographic examinations help in the diagnosis as do X-ray after an opaque meal.

It should be remembered when trying to estimate the size of the liver that in a definite number of patients the liver is bound to the diaphragm from adhesions due to perihepatitis and therefore we do not see the usual respiratory excursion of the liver.

Where any of the above complexes occur in a patient with a positive Wassermann the patient should have the appropriate treatment and in the large majority of cases this will clear up the diagnosis.

The Wassermann was found positive in 90% of such cases by Stokes.[44] In the remaining 10% where it is suspected a carefully taken history, a thorough examination and the employment of some of the other blood tests for syphilis will usually make the diagnosis evident. Even where it is only suspected the therapeutic test should be employed.

Prognosis.

The prognosis in any one case varies with the proportion of the types of lesions present. It also varies with the general condition of the patient and his tolerance of treatment and with the amount of treatment he receives. Speaking generally the prognosis in syphilitic cirrhosis is bad as healing occurs by contraction of the fibrous tissue and consequent pressure on the surrounded tissue. Even with careful treatment this tends to happen. Despite this Edwards[45] cites two cases of advanced cirrhosis which recovered completely under iodides.

Gummata of the liver may respond quite readily to antisyphilitic treatment, and therefore the prognosis is better than in syphilitic cirrhosis, and some of the conditions simulating gummata especially carcinoma.

The prognosis where cicatrices have formed is

bad as once this condition is established no treatment will affect them.

Treatment.

For the treatment of gummata and cirrhosis Thomson[46] relies on mercury and iodides which he advocates to be "pushed with great vigour preferably intravenously." He dismissed arsenic by saying that if it is given at all it should be administered with great caution. I make no apology for turning again to Stokes[47] for help in the treatment of this condition as he gives the most rational outline of the course of treatment to be employed, and I shall quote his treatment at the end of this section. Too hasty and too energetic therapeutic measures are apt to lead to disaster in late syphilitic hepatitis. The therapist has been advised to give due heed to the act of therapeutic coddling and restrain his desire for arsenic miracles.

When the diagnosis of syphilis is made a large proportion of cases will respond well immediately and ultimately to the employment of arsenic. The effect of the arsenic as a tonic and in clearing up the systemic syphilis gives the patient a feeling of well being which he has not experienced for years but there is always, in a certain proportion, the unpredictable element contingent on the proportion of diffuse to localised syphilitic infiltration.

It is towards the end of the first course or in two or three months immediately following that the

mistake in using arsenic at the onset becomes apparent in the form of increasing abdominal distension due to ascites. The administration of arsenic at the outset to patients with jaundice or with even a small amount of ascitic fluid may be a mistake of the first order as has been shown by the experience of syphilologists.

The Herxheimer reaction results in an immediate increase in fluid and with the ensuing contraction of the liver the circulatory disturbance becomes fully established and the patient is wrecked.

Jaundice is seldon perpetuated if the patient escapes the first violent reaction. Keeping these risks of a Therapeutic Paradox in mind and with the uncertainty of the exact state of the liver,

mercurial and iodide preparation is the safe and ideal approach to treatment in the majority of cases.

If the case be of long standing or if there is any sign of fluid or of insidious onset it is best to start treatment in hospital under constant observation and give a period of two or three months of cautious treatment for the first course as follows:-

First week or two potassium iodide by mouth 1-2 gms. three times a day if tolerated and Mercury with chalk 1 or 2 grains three times a day.

Second to 4th week inunctions in addition 4 gms. 30grs. clean. During this period iodide may be

given intravenously if the patient's condition is good or his gastro-intestinal tolerance poor. The dose being from 3-8 gms. daily or every other day.

4th - 6th Week if progress is slow and there are no unfavourable signs from the Kidneys, succinimid intramuscularly or the bichloride may be substituted for other mercurialization, the iodide being continued.

Depending on the response but in general not before the 8th week if progress is favourable the mercurialization and iodide may be discontinued and neo-salvarsan intravenously substituted in doses of 0.2 - 0.6. Gms. to the dosage scale of 1 decigram for each 25 lbs of body weight.

If well tolerated six small injections may be given at weekly intervals. The patient is then placed on a rest period of from 1 to 2 months using Mercury and Chalk and iodides ad interim.

Further courses of treatment depend on the patient's progress. Some patients stand arsenic so poorly that they require months of rest between courses and liberal use of mercury and iodide. However the ultimate effect of arsenic seems to be good.

Most patients are able to carry on with an ordinary second and third course of from 6 to 8 injections with four months intervals between courses without incident. Patient's should be impressed with the great importance of observation and of observing their treatment intervals which their

sense of well being and striking improvement may lead them to neglect. Only in this way can a certain proportion be protected from the development of serious relapse or of other manifestations of syphilis. A follow up system is as necessary in visceral as in early syphilis.

IV. Chronic interstitial Pericellular Cirrhosis of Heredosyphilis.

As this paper is a clinical review of hepatic syphilis and not in any sense a treatise on Pathology, I shall not deal fully with this condition. The name in itself provides a picture of the pathology. The clinical aspect of the disease in no way differs from that of the late types of syphilitic hepatitis just described except that it comes on in younger subjects who are congenital syphilitics.

The treatment of the condition is the same as that of the diffuse cirrhosis of acquired syphilis except that the dosage of drugs must be moderated to suit the age and weight of the patient.

In concluding this section I should like to say that my idea in this first part of the paper has been to collect the opinions of recognised authorities on the subject of hepatic syphilis and combine these to give a concise clinical picture of the condition.

The descriptions of hepatic syphilis in text books of Syphilis, and more so in General Medical Text Books, are so brief and incomplete that I feel such a scheme as this is necessary in order to have a clearer idea

of the subject before going on to the review of my cases.

Certain collateral factors appear in the management of patients with syphilitic hepatitis, some of which are peculiar to this condition, while others occur in different types of syphilis.

In order not to confuse the issue I have omitted these from this section and will deal with them, as they arise in the cases, in the concluding section which will take the form of a discussion of the cases.

PART II

Review of 14 illustrative cases of

Hepatic Syphilis.

EARLY BENIGN ACUTE HEPATITIS.

B. 9995 27 - 6 - 33.

This patient was a man aged 32 years, who was living apart from his wife.

He was exposed to infection 3 weeks previously and reported with an ulcer on his prepuce of 1 week duration.

He had no history of any previous venereal disease, and had had no treatment.

On examination he was found to have a phimosis. He had a profuse sero-purulent discharge from his sub-preputial area and ulceration of the exposed part of his prepuce.

He had marked inguinal adenites on both sides. He had no lesions of the skin, mouth or anus and no generalised adenitis.

He had no abnormalities of his other systems.

Dark ground examination revealed spirochaeta pallida from the ulcers and his blood Wassermann reaction was already strongly positive.

He was accordingly put on a course of NK - Bismuth being withheld for two occasions till he had septic teeth removed.

After he attended thrice getting in all 0.9 gms NK and .3 gms. Bismuth he ceased attending from the 15 -7 -32 till 1 -XI -32.

He was written to in October and returned on 1st November.

When he returned he was jaundiced and his liver was found to be 1" below the costal margin.

He had been jaundiced for several weeks and treatment by his own doctor failed to alleviate the condition. He stated he had never felt ill or had any intestinal upset.

He was given 20 c.c's. glucose intravenously 0.1gm NK and 0.2 gms Bis twice a week and the jauddice and bile in his urine gradually became less till it had disappeared within 3 weeks.

The course was continued up till 7 -3 -33 giving in all 4.0 gms. NK and 3.9 gms. Bismuth. He had four weeks rest and on return his blood Wassermann was reduced giving a weak positive result.

He was put on another course of dual therapy and when examined at the end of June his Liver was not below the costal margin. By August 1933 his blood Wassermann reaction had become negative.

Discussion.

There is no doubt as to the diagnosis of Syphilis in this case.

His interrupting of his first course, only getting 0.9 gms of arsenic and 0.3 gms of Bismuth, did not allow of sterilisation of his blood which was undoubtedly infected as judged by his Wassermann Reaction.

His jaundice coming on as it did within 4 months of infection with the little treatment made one suspicious as to its aetiology. The fact that it did not respond to the usual measures for catarrhal jaundice and its symptomless nature put one more on

ones guard. It was therefore decided to try the therapeutic test. Instead of getting worse as it probably would have done if it had been catarrhal it started to improve straight away and cleared up remarkably quickly. The liver returned to normal size and no ill effects were seen on further administration of arsenic. This case seems to be without doubt an Acute Benign Syphilitic Hepatitis coming on as some do rather later in the disease than usual.

A. 4386 Stoke 20th. Nov. 1934.

This patient a man aged 27 years first attended the Stoke Municipal Clinic on the above date because of a sore on his penis.

The sore had been present for about one month and he gave a history of exposures to infection one month and two months previous to his attending the clinic.

On examination he was found to have a typical Hunterian chancre with inguinal adenitis on both sides. Spirochaeta Pallida were found in the serum expressed from the sore and the Wassermann reaction gave a strongly positive result.

He showed no other signs of syphilis.

Treatment was started that day and within a week he was given 1.35 gms. of "914" and 0.6 gms of Bismuth Metal.

He then defaulted from treatment. He was written to on February 7th and returned to the clinic on the 1st of March.

When he presented himself on this date, he was markedly jaundiced. His skin and conjunctivae were a deep yellow colour. His urine showed the presence of bile but his stools were not pale in colour.

His liver was uniformly enlarged to about one inch below the costal margin. The edge was smooth and the organ was not tender. The gall-bladder was not palpable and there was no tenderness on palpation over the gall bladder region. The patient was completely

free from symptoms.

He had been put on light diet by his own doctor and treated as a case of Catarrhal Jaundice for a fortnight without any beneficial results. His appetite was good in fact he complained of feeling hungry while on his light diet.

On March 1st and 5th he was given intravenous injections of 0.6 gms and 0.75 gms. of Ametox which is a proprietory form of Sodium Thio Sulphate.

On March 8th and 12th he was again given Ametox intravenously and 0.15 gms. of Kharsulphan intramuscularly.

Discussion.

This case was under the care of the Venereal Diseases Officer for Stoke-on-Trent who asked me to see the patient with him.

We came to the conclusion that it was a case of Syphilitic Hepatitis.

Arsenic as a cause of the Jaundice could be ruled out on the grounds that only 1.35 gms. had been given and that four months had elapsed between the last arsenical injection and the occurrence of the jaundice.

The symptomless nature of the jaundice and the lack of response to the measures employed by his own doctor are strong evidence against it being catarrhal in nature. The patient felt better after his two injections of arsenic and this backs up our diagnosis of it being syphilitic in nature.

I am of the opinion that this is a case of Acute Benign Syphilitic Hepatitis coming on six months after the original infection.

The delay in onset is probably explained by the fact that the infection was temporarily held in check by the treatment given when the patient first reported. The infection then established itself again and increasing in intensity precipitated this attack of Hepatitis.

Patient "A B" Stafford aet 16 yrs. Feb. 1935.

This patient was a girl who was in a home for girls in Stafford. On admission in November 1934 she was found to have a vaginal discharge which proved to be gonorrhoea. She admitted exposure to infection about 10 days previously. A Wassermann Reaction was done as a routine but was negative and it was not repeated.

She was given treatment for her cervicitis and this reacted quite well to treatment. At the end of January she developed Jaundice and simultaneously with it a profuse macular rash. The doctor in charge of the home called me in in consultation.

The patient felt perfectly well her appetite was good and she had no complaints. When I examined her I found she was moderately jaundiced she had a typical syphilitic rash, general adenitis and mucous patches in her mouth. She was obviously in the florid secondary stage of syphilis. Her liver was just palpable below the ribs.

No primary sore had been detected during her treatment for gonorrhoea.

Her Wassermann Reaction was now strongly positive.

I advised that the patient be given dual therapy with arsenic, and Bismuth. She was given 0.2 gms of Bismuth metal weekly and the arsenic was divided into 0.15 gm. doses intravenously twice a week.

The rash had faded after two doses and the jaundice had practically disappeared at the end of a

fortnight and had quite gone in three weeks.

Since then the usual course of treatment has been continued with no bad results.

Discussion.

There was little doubt as to the aetiology of the Jaundice in this case. The skin rash the adenitis and the mucous patches all pointed to the presence of a very active syphilitic infection being present.

The diagnosis of Acute Benign Syphilitic Hepatitis was bourne out by the response shown to treatment and the added feeling of well being which the patient enjoyed during treatment.

This case teaches several interesting lessons.

The first is the way in which a single Wassermann Reaction can be misleading. The blood test should have been repeated at intervals from the date of exposure till the end of the incubation period for syphilis - at least three and a half months.

It also shows the difficulty in finding the primary sore in some cases especially in the female where it may be situated on the cervix.

It is quite possible that a primary sore on the cervix may have been dismissed in this case as being merely erosion caused by the gonococcal infection.

It further demonstrates that when the diagnosis has been made we must have courage to carry out the appropriate treatment straight away to get the best results.

1025. Ward 20. 17 -10 -29.

This woman aet 30 yrs reported complaining of a leucorrhoeal discharge for 2 months having been exposed to infection one month previously.

She had become jaundiced one month before reporting and still showed an icteric tinge and at the same time she developed a rash.

On examination she was found to have inguinal adenitis on both sides.

She had a well marked roseolar rash on her trunk and limbs.

Her skin and conjunctivae were very jaundiced.

Her liver was uniformly enlarged about 1 inch below the costal margin, and she had pain and tenderness on palpation in the right hypochondrium.

Her urine contained bile.

No abnormality was detected in any other system.

Her blood Wassermann was strongly positive.

She was given 20 c.c's of Glucose every day and small doses of NK every second day starting with .05 gms.

In 5 days her urine was free from bile and in 9 days the jaundice and rash had completely disappeared.

Towards the end of the course she was given bismuth, and by the end of the first course on 6 - 1 - 30 she had received 3.5 gms NK and 2.45 gms. Bismuth.

In February after her rest her blood Wassermann had become negative. Her liver had returned to

normal size.

She continued treatment up till September 1932 having in all 9.95 gms NK and 19 gms. Bismuth. Her Wassermann Reaction remained negative and her cerebro spinal fluid was also negative.

She never had any further evidence of liver involvements.

Discussion.

This case presents the typical picture of the Early Benign Hepatitis of Syphilis.

She showed the secondary roseolar rash with the jaundice and enlarged liver along with a strongly positive Wassermann Reaction.

All these findings came on at the expected time - 2 months after the date of infection. The jaundice failed to clear up when untreated and responded like magic to treatment with Neokharisivan.

The enlargement of the liver disappeared and no subsequent trouble was given by it.

The patient tolerated treatment well and her blood Wassermann remained negative throughout, after the first course.

Had the jaundice been caused by anything else than syphilis the administration of arsenic would certainly have aggravated the condition and we would have had further trouble during the remainder of her treatment.

Syphilitic Destructive Hepatitis.

B 1940.

This was a male patient of 51 yrs. of age who was admitted to a Medical Ward desperately ill.

He gave a history of an ulceration of his leg 20 years ago.

The history of his family was that he had 6 children alive and well but that his wife had several miscarriages between healthy children.

Examination revealed a gumma on the inner aspect of the lower third of his left leg.

There were old indurated scars on the coronal sulcus of his penis and on the frenum.

He showed definite jaundice and his conjunctivae had a yellow tinge. He had boarding of the upper third of his right rectus muscle over his gall bladder region.

His liver was diminished in size. He had no splenic enlargement. Examination of his heart revealed systolic and diastolis murmurs in both the mitral and aortic areas.

His urine which was high coloured and specific gravity of 1032, contained leucine and Tyrosine crystals.

Central Nervous System - No abnormality. His blood Wassermann reaction was weak positive.

He died within 24 hours of admission to Ward 5A and had never received any antisyphilitic treatment.

Discussion.

From the history there can be little doubt as to

the patient suffering from syphilis. This was borne out by the finding of scars, the presence of gummata. The aortic heart lesion, and the positive Wassermann Reaction.

The presence of the icteric tinge and the finding of leucine and tyrosine crystals in the urine point to a liver atrophy.

A post-mortem examination was carried out and the report as to the cause of death was "Atrophic Cirrhosis of Liver most probably of syphilitic origin."

I think that there can be little doubt that this patient suffered from the late Diffuse Syphilitic Hepatitis.

Probably had he been seen 10 or 15 years earlier his liver would have been enlarged.

This is one of the terminal results of Diffuse Syphilitic Hepatitis the development of an Acute Yellow Atrophy.

7125 26 years. 15 -11 -28.

This patient was attending Ward 20 with a resistant gonococcal infection of the urethra when it was found on 12 -6 -30 that she had a primary sore on the cervix.

She admitted exposure to infection 14 days previous with her fiancé.

Her Wassermann Reaction was negative but Sp. Pall were found on dark ground. She was given .15 NK and .3KSP and the Wassermann reaction repeated the next week returned a doubtful negative result.

She had 3 further injections of .3 NK and with the 4th on 24 -7 -30 she had a vaso-dilator reaction. Adrenalin in MV. She was now married to the person from whom she contracted Syphilis.

13 -7 -30 .15 KSP

14 -8 -30 .2 KSP

6 -11 -30 reported MP. 2 weeks overdue.

13 -11-30 Wassermann Reaction negative

27 -11-30 3.15 KSP

4 -12 -30 Examined - Pregnant. To have 5 Bismuth then As. .15 Bismuth.

12 -12-30 Transferred to Royal Maternity Hospital continued 2 months pregnant.

In Ward 24 in Feb. 12 days with Acute Yellow Atrophy Pregnancy terminated with beneficial results.

18 -6 -31 Wassermann Reaction negative No icterus.

2 -7 -31 Feeling fairly fit. Report 2 months.

10 -9 -31 Wassermann Reaction negative. Looking V. well Pulse 72 regular. Reflexes present and equal.

24 -9 -31 Report 3 months.

4 -2 -32 Wassermann Reaction negative. To report 3 months. Reflexes OK.

12 -5 -32 MP. one week overdue usually regular. Report 2 weeks if no MP.

Wassermann Reaction negative. If MP. report 3 months.

8 - 9 -32 2 months pregnant Royal Maternity Hospital Sent to 20 to have Dr. Liston's opinion if patient's liver is healthy enough for pregnancy to be continued.

Feels faint. Sleeps well. Eats well.

Defaulted from treatment.

Discussion.

There can be no doubt that this patient developed syphilis when spirochaetes were isolated from her cervical sore. She was a sero-negative case when treatment was first started but a doubtful negative result was returned one week later which indicated a blood infection.

She had four intra-venous arsenical infections and after the last had a vaso-dilator reaction.

Her treatment was continued with small doses of intra-muscular arsenic, the amount given having to be kept low on account of her intolerance to the intra-venous administration.

She became pregnant and was transferred to the Royal Maternity Hospital. While there she developed signs of Acute Yellow Atrophy. Leucin and tyrosine crystals were found in the urine and the liver shrank

under the costal margin. It was decided that the Atrophy was caused by Syphilis as she had received inadequate treatment and that the condition was aggravated by the pregnancy.

Her antisyphilitic treatment was continued and her pregnancy terminated. Contrary to expectation the patient recovered.

Her history has been given in a tabulated form as it is very striking.

The patient appeared to be on the point of death when she was admitted to the Maternity Hospital and her recovery under the administration of arsenical drugs seems to clinch the diagnosis that the Yellow Atrophy was syphilitic in origin.

This case is not only striking because it is a case of recovery from Destructive Hepatitis but also because in 1932 she again became pregnant and showed no signs of liver insufficiency. The pregnancy was allowed to go on to term and had a normal course.

Mild Chronic Hepatitis of Latency.

C 446 16 -9 -32.

This male patient was aged 58 years and gave a history of a sore on his penis at the age of 19 years.

His complaint now was weakness of his legs for 20 years, and he was transferred to Ward 5A from a Medical Ward because of the findings in his cerebro spinal fluid which were:-

Cell Count	6 per. cmm.
Globulin	Increased a trace.
W.R.	Weak positive
Col. Gold Curve	0122100000.

He was married but his family history was not suggestive.

On examination no scar was seen and he had no adenitis or skin lesions.

He had haemorrhoids which had been there for about 10 years.

His cardio-vascular and respiratory systems showed no abnormality. Examining his Central Nervous System the following were the findings.

Pupils	Equal. Margins slightly irregular. Reacted to "light" and accomodation.
Knee Jerks	Present and active.
Ankle Jerks	Could not be elicited.
Rombergism	Marked swaying.

He complained of weakness of the left leg and arm.

He had marked intention tremor and slurring speech. No nystagmus or seneory loss could be made out.

His liver was found to be uniformly enlarged the edge was about 1½" inches below the costal margin.

His spleen was not enlarged to palpation or to

percussion.

His blood Wassermann Reaction was negative.

After having his optic discs examined he was put on treatment with Tryparsamide, Bismuth and iodides.

About 6 weeks after the commencement of treatment he complained of epigastric pain radiating from the right side.

In 9 months he received three courses of treatment totalling 52 gms. T.P.A.

6.4 gms. Bismuth, and iodides during the first course and for fourteen days during each months rest.

When he was examined at the end of this time in June 1933. He had put on weight, about half a stone, His Rombergism was reduced to a very slight swaying and the weakness of his left arm and leg has completely disappeared and his Cerebro Spinal Fluid Wassermann had become negative.

His liver was now reduced in size to under the costal margin.

Discussion.

This case was definitely one of syphilis of the Central Nervous System with a negative blood Wassermann which is found in a definite proportion of cases.

The enlarged liver was found incidently, or accidentally in the routine examination. He never had any symptoms indicating liver involvement and the only sign at all referable to portal obstruction was

the presence of haemorrhoids.

The treatment he received was aimed at the amelioration of the Nervous condition and its efficacy has been proved by the findings after 9 months.

The attack of abdominal pain during the first course was explained away by a gastric crisis due to the Central Nervous lesion. Although it could not be proved it may have been hepatic in origin due to a mild Herxheimer reaction from the early administration of arsenic.

This symptomless hepatic enlargement in a syphilitic patient with a negative blood Wassermann reaction seems to point to the liver being the seat of a Mild Chronic Hepatitis of Latency.

It is especially interesting to see how well the liver responded to treatment with Iodides, Bismuths and the prevalent arsenical Tryparsamide.

C 115 18 - 7 - 32.

This was a married man who was recommended to 5A as his wife was a patient in Ward 20 suffering from Central Nervous syphilis.

He was aged 58 years.

He had been married 33 years and had 3 of a family a son aged 32 years who was backward and 2 daughters aged 30 and 28 both married and healthy. He gave a history of having a rash on his face, and spots on his penis when he was a young man.

He had a large oval scar on his glans penis and some leucoplakia on the buccal mucous membrane on both sides but apart from this there was no other clinical evidence of Syphilis.

His blood Wassermann Reaction was strongly positive 18 -7 -32. He received between then and the 8 -8 -32 1.2 gms. NK and .9 Bismuth when he ceased attending. He reported on 14 -11 -32 Jaundiced his liver being about 1½" below his costal margin. He stated he had been jaundiced for 14 days and treated by his own doctor. He felt quite well and had no chill or exposure to cold.

He was given Sodium Thiosulphate and 20 c.c. glucose but reported again 4 days later with the Jaundice deepening and his urine showing much more bile.

He was then given small doses of NK .1 gm. in all four injections in a fortnight within which time his jaundice disappeared and his liver was just palpable below the costal margin.

He stayed away for 2 months but commenced another course of small doses of NK and Bismuth.

In this course he had 1.4 NK and 5.9 Bismuth and showed no intolerance to the drugs.

Examined on 29 -6 -33 his liver was under the costal margin and his spleen not enlarged. His Wassermann Reaction was still strong positive.

Discussion

This man was a long standing case of syphilis. No enlargement of his liver was noted on first examination.

He received 1.2 gms NK and .9 Bismuth only, before he showed his jaundice and enlargement of the liver.

The jaundice did not respond to treatment of catarrhal jaundice given by his own doctor, nor was it accompanied by the usual symptoms of catarrhal jaundice.

The facts that he had so little arsenic prior to the jaundice and that he showed no intolerance to arsenic subsequent to the jaundice makes it impossible to believe that Arsenic alone was the cause of the liver upset.

The rapid improvement when arsenic was exhibited makes it highly probable that the liver condition was due to syphilis, as it is well known that arsenic makes catarrhal jaundice worse.

My interpretation of this case is that there were probably two factors at work. The patient had probably a latent syphilitic hepatitis which was

actuated by the arsenical drugs to begin with in a Herxheimer flare up and that the further giving of arsenic put a stop to the condition.

C 1668 16 - 5 - 33.

This patient a man aged 47 years was referred to Ward 5A solely because of a leucoplakia of the tongue and angles of the mouth.

On enquiring he admitted having a sore on his penis 30 years ago when he had a short course of treatment with medicine.

He stated that he was never jaundiced nor had he ever any rashes on his skin. He has one grown up daughter and his wife never had any miscarriages.

He had no sign of any lesions, past or present on his skin and he had no glandular enlargement.

He certainly had leucoplakia of his buccal mucosa and of his tongue which was cracked and sore.

His Central Nervous System examination was negative except that his pupils were small. They were regular in outline and react to Light and Accommodation.

His heart was not dilated and all the sounds were closed. The second aortic sound was slightly accentuated.

His liver was found to be uniformly enlarged to about ¾ of an inch below his costal margin. It was firm in consistence and the edge was regular.

His spleen was not enlarged.

A note was made of the myotic pupils and he is to have his discs examined at the end of his first course of treatment and a Lumbar puncture performed to see the state of his cerebro spinal fluid. This

would have been done before commencing treatment but it was not convenient for the patient to lie in bed for 48 hours after the Lumbar puncture.

His Wassermann Reaction was triple positive and his Sachs Georgi test positive.

The patient was put on NK and Bismuth and given Sodium Iodide gr XV thrice daily by mouth and Boroglyceride as a local application.

In six weeks he received 2.55 gms. NK and 1.8 gms. Bismuth and the Iodides. His liver now was just palpable under the costal margin and the patient felt and looked very well.

Discussion.

The only subjective phenomenon which the patient had on first being seen was pain in his tongue.

He never had any trouble pointing to liver disease. He had a definite history of infection, the scar remained to tell the tale, and his Blood Tests for Syphilis were both positive.

He had no alcoholic history and we assumed his liver enlargement to be due to Syphilis. He had no ascites, nor haemorrhoids and his liver was quite symptomless.

The response made to the Iodides and arsenic in diminution in size of his liver was remarkable in such a short time.

The evidence seems to point to this being a case of Mild Chronic Hepatitis of Latency.

Diffuse and Localised Gummatous Hepatitis.

Perihepatitis

Chronic Interstitial Pericellular Cirrhosis

of Heredosyphilis.

9542 Female aged 45 years 2 - 7 - 31.

This patient had been married 24 years. Her husband was killed in the War.

She had 5 children all born alive - the second last one died aged 7 weeks - cause unknown. One other died of diphtheria. The others are alive and well and have no stigmata of congenital syphilis.

She was perfectly well up till 3 years prior to first attendance when she started to complain of pain after food and sickness. This was so constant that a Gastric Ulcer was suspected and an exploratory laparotomy performed. No cause for the complaints could be found.

She had no further complaint till one month before she attended the clinic when a mass was felt in the right hypochondrium. She was again operated on and a large mass of granular tissue revealed in the liver. A portion was removed and a biopsy performed this proved to be gummatous in nature.

A Wassermann Reaction was done and the result strongly positive.

On examination at the Clinic the patient was found to have an enlarged liver. The enlargement stretched from the left hypochondrium across the mid-line where it reached 4" below the ziphisternum to the 9th costal cartilage. It was a fairly firm mass - painless and moved on respiration. There was no free fluid in the abdomen.

The cardio -vascular system showed no abnormality

and the central nervous system did not show any lesion.

A complete blood examination - blood chemistry and count gave negative findings. The urine showed no abnormality.

Treatment was started at the Clinic on 1 -7 -31 after she had been given Iodides in the Surgical Ward for 3 weeks.

The iodides were continued and small doses of Arsenic were given intra-muscularly with glucose intra-venously.

By 9 -12 -31 she had received 2.85 gms of Kharsulphan and Iodides. She was given a fortnight with iodides alone and then a further 14 days with no treatment and reported on 6 -1 -32.

The Wassermann reaction was still strongly positive.

The liver had shrunk about 1 inch in the 5 months.

The treatment was continued in small doses and bismuth was also administered in moderate doses.

The treatment was continued until 7 -6 -33 when the patient was lost sight of. She had received in all 8.85 gms. of Kharsulphan and 4.35 gms. Bismuth which represented only a moderate amount of treatment in 18 months.

The liver had gone down to about 1 inch from the costal margin and the cause of defaulting was probably that the patient felt so well as she said she did, that she considered the long term of treatment irksome and unnecessary.

The Wassermann Reaction remained strongly positive throughout.

Discussion.

This is a clear cut case of syphilis of the liver where the lesion was not only seen naked eye but confirmed microscopically.

The lesion was gummatous in nature as seen at the operation and was very extensive.

The pain and vomiting in this case were interesting symptoms. Their resemblance to the symptoms of gastric ulcer or duodenal ulcer was so marked that two operations were performed without it being thought necessary to do either a gastric analysis or to take an X-ray photograph.

The Wassermann Reaction which would have acted as a pointer was omitted till after the second operation, when the condition was obvious.

Judging from the history of the patient it seems likely that the syphilis was acquired many years before the liver involvement became noticeable and this is to some extent borne out by the persistently strongly positive Wassermann Reaction.

The Wassermann Reaction seems more difficult to change in visceral syphilis than in any other type of the disease.

The diagnosis having been made beyond doubt the determining of the lines of treatment was easy.

This being a single gummatous lesion with little or no diffuse cirrhosis. This conclusion was come

to as there were no obvious signs of any portal obstruction or impairment of hepatic function.

The pain and vomiting of which the patient complained were probably indications that the gummatous process had reached and involved the peritoneum.

The patient was started on treatment by being given a course of iodides to soften and vascularise the scar tissue surrounding the gumma - this was followed by intra-muscular arsenic. The intra-muscular route being preferred because of its giving a prolonged effect rather than the rapid sterilising effect of the intra-venous drug which is quickly excreted.

The arsenical treatment was backed up by glucose intra-venously with a view to keeping up the glycogen supply in the liver and save it to some extent from the toxic effect of the arsenic. Bismuth was withheld for a while to save the liver. The good progress of the case - the alleviation of symptoms and the return of the liver to approximately its normal size justified the lines of treatment adopted. No unforseen accident occurred as a result of the therapy given.

Mrs P. 919.

This woman aet 37 years had been married 12 years and was first seen in April 1929.

She had two children aged 11 and 10 years who were alive and healthy without any signs of specific disease. She had no miscarriages or still berths.

Her first complaint was pain in the epigastrium. This pain was almost constantly there but was much worse after food. She had occasional vomiting.

This started four years prior to her coming under our care and she suffered this discomfort for 2 years when she was operated on in Kirkcaldy Hospital. A gastric ulcer was suspected but the suspicion proved at operation to be false.

She continued to suffer for a further 2 years until she sought advice at the Royal Infirmary and was admitted to a medical ward.

Here she was discovered to have a strongly positive Wassermann Reaction and she was transferred to Pilton Hospital under the care of Mr. Lees.

Clinical examination revealed no abnormality of the Central Nervous System or of the Cardio-Vascular system.

No evidence of an old primary syphilitic lesion was detected. The blood Wassermann Reaction was confirmed.

The history of the patient was as given above. Her tongue was moist and clear, her remaining teeth in the lower jaw were in bad condition.

Her liver was found to be markedly enlarged.

It extended to about 4" below the costal margin. It was fairly firm and quite smooth, the edge being easily defined.

The spleen which was a little soft was just palpable below the costal margin.

A complete blood examination was performed and there was no abnormality present.

She was started on treatment on 12 April 1929 when she was given .2 gms. Bismuth biweekly and K.I. gr. XV T.I.D.

The pot. iod. had to be stopped due to sickness but the bismuth was continued until the 24th May. On the 16th May she complained of upper abdominal pain and sickness. On this date the patient had a severe haematemesis. She was transferred back to the Medical Ward in the Royal Infirmary from which she had been admitted, where antisyphilitic treatment was suspended.

She re-appeared for treatment at Pilton Hospital in October when her liver was still 4" below the costal margin.

She was given tri-weekly intramuscular doses of .1 gm. Bismuth with 20 cc. glucose intra-venously, and also Sodium Iodide intra-venously.

This course she tolerated well and on terminating it on 13th January, 1930 she had had 3.95 gms. Bismuth and 80 cc's Nal.

At the beginning of her next course in February

her Blood Wassermann Reaction was still strongly positive.

She was given a course of "914" with glucose and insulin in all 2.7 gms. of NK. On examination after her months rest in May her Wassermann Reastion was strongly positive. Her liver was reduced in size to 1" below the costal margin and her spleen was well under the costal margin.

Since then she has had courses of treatment which have been interrupted by non-attendance. Her total treatment has been

NK	6.1 gms.
Bismuth Metal	9.25 gms.
Bivatol	20 c.c's.
Sodium Iodide	120 c.c's.

Her blood Wassermann Reaction in June 1931 was weak positive but when she was last seen in June 1932 it was strong positive.

She had repeated blood examinations done, none of which showed any abnormality. Her blood count on the 27 -7 -31 which was typical of the others was.

R.B.C's.	4,770,000
HB..	90%
C.I.	.9
W B C's.	5,200
Poly's	68%
Eosin	1%
Large Lymph.	10%
Small Lymph.	18%
Mononuclear	3%

Her liver remained constant in size enlarged to 1" below the costal margin and firm in consistance. Her spleen was not enlarged to palpation and only slightly so to percussion.

Discussion

The initial history of this case made it look like one of gastric ulcer but that diagnosis was disproved by operation at Kirkcaldy Hospital.

She was thoroughly overhauled in the Medical Ward in the Infirmary and the conclusion come to that her condition was purely syphilitic.

Her Wassermann reaction raised suspicion, and the negative blood findings pointed to it being a syphilitic hepatitis. The attack of abdominal pain while in Pilton Hospital probably pointed to an involvement of the peritoneum, and the haematemesis was in all probability due to varix at the lower end of the oesophagus from interference in the portal circulation. This may have been made worse on treatment being administered as iodides were not well tolerated.

The rapid improvement in the condition of the liver and the complete disappearance of symptoms when the patient could stand and got adequate and appropriate treatment i.e. NK and NAI seem to make the daignosis of syphilis of the liver quite definite.

C. 99.

This male patient aged 50 years was admitted to a Medical Ward in the Infirmary complaining of a feeling of weight in the abdomen especially in the left hypochrondrium which he had felt for 2 years.

He gave a definite history of venereal disease in 1918 when he was in the army. He was treated at that time in Robroyston Hospital in Glasgow with irrigations only.

In the Medical Ward it was found that the feeling of weight in the abdomen was due to a great enlargement of his liver and spleen. He was thoroughly examined in that ward, and as his blood count and blood picture were quite normal and as his blood Wassermann was strongly positive he was referred to Ward 5A.

His family history was that he had one son aged 16 years, the only pregnancy, that was prior to the date of his infection.

Examination revealed scarring at his urinary meatus and slight adenitis in the right groin.

He had a purpuric rash of both legs especially marked at his left ankle and foot. He had no general adenitis, his buccal mucous membrane was clear and his cardio-vascular and Central Nervous Systems showed no abnormality.

His liver was enlarged down to his umbilicus. The surface and edge were smooth - no irregularities could be felt and the enlargement was uniform

throughout the whole organ. It was firm to the feel. His spleen was also enlarged about 2 finger breadths below his costal margin, and also smooth and firm in consistence. He had a little free fluid in the peritoneal cavity.

His Wassermann reaction was repeated and found to be strongly positive.

He was offerred a bed in the Ward but declined.

He was accordingly started on treatment being given Potassium Iodide gr. 20 thrice daily and 0.1gms Bismuth biweekly.

After one months treatment he developed a pustular rash and the iodides had to be discontinued.

The next week he was started on small doses of Neokharsivan .15 gms. with 10 c.c's Glucose intravenously along with the Bismuth intramuscularly.

In the first course he received, as well as the iodides, 1.35 gms NK and 3.3 gms. Bismuth.

He had a months rest from all treatment and on return at the end of December his Wassermann Reaction was still strongly positive.

His liver was reduced in size and his spleen was 1 finger breadth below the costal margin. There was no detectable ascites.

He received another course of NK and Bismuth in all 2.7 gms NK and 2.4 gms Bismuth up to 17 -3 -33.

On 14 -4 -33 his Wassermann Reaction was positive. He felt very much better. His liver was 2 finger breadths above the umbilicus and his spleen was

just palpable on deep inspirations.

He was given a further course, this time of 0.3 gms NK weekly and Iodides in a mixture with Lig. Arsenicalis and he had no further intolerance to the iodides.

In his third course ending on 26 -6 -33 he was given 3.0 gms NK and 3.9 gms Bismuth.

His liver was now reduced to 2" below the costal margin and his spleen was the same as at the last examination.

He does not now complain of the feeling of weight in his abdomen. His general condition is very ggod as might be judged by the fact that his weight has increased since he started treatment from 9 st.12½lbs. to 10 st. 8 lbs.

Wassermann Reaction was still strongly positive after his rest.

Discussion.

In this case the diagnosis of Hepatic Syphilis was made in the Medical ward, by as far as possible excluding all other conditions giving such hepatic and splenic enlargement. The strongly positive Wassermann Reaction also pointed to this diagnosis.

The ascites, without other signs of portal embarrassment was probably due to a perihepatitis and peritonitis of specific origin.

The patient received the appropriate treatment starting with iodides and Bismuth and then after about

6 weeks starting cautiously with arsenic.

The arsenic was well borne without any signs of liver damage such as jaundice. The extremely good clinical condition of the patient after treatment and the gradual diminution in size of the liver and spleen seems to confirm the diagnosis.

From the character of the liver I should be inclined to describe it as a diffuse type of gummatous hepatitis accompanied of course by some Interstitial fibrosis.

It seems highly probable that the patient will continue his treatment without any very serious set backs for with the rational lines on which he has been treated, it is unlikely that he will show any signs of a Therapeutic paradox.

A. 519 Female aged 18 years 15 -8 -32.

This patient had been in a Medical Ward 6 months ago when her complaints were dull epigastric pain, a feeling of weight in the abdomen, and attacks of epistaxis. The day prior to admission she vomited "coffee ground" material.

On examination her spleen was found to be 2" below the costal margin and her liver 1" below the costal margin. Her blood Wassermann was strongly positive.

At this time her blood count was:-

R.B.C's	3,700,000
Col. Index	.5
W B C's	4,500
Polymorphs	60%
Lymphocytes	39%
Eosinophils	1%

She was given potassium iodide and the notes say this was followed by a considerable reduction in the size of the spleen.

She was transferred to the Astley Ainslie on 29 -4 -32 where she seemed to make good progress until 10 -5 -32 when she had a haematemesis and developed a swinging temperature.

Her blood count on 30 -5 -32 was:-

R.B.C's	2,290,000
Col. Index	.45
W.B.C's	3,500

She picked up again and on 3 -6 -32 her count was:

R.B.C's	3,500,000
C.l.	.34
W.B.C's	4,600.

There was no lymphocytosis seen.

She was transferred to Ward 14 on 20 -7 -32 as a

case of Splenic Anaemia with Congenital Syphilis. A splenectomy was performed three days later. The patient lost a lot of blood from large veins from the spleen to the diaphragm, and was given a transfusion of 18 ozs. on the table.

The patient made a good recovery from the operation and was referred to Ward 20 in 15 -8 -32. She was anaemic and it was considered best that she should go home for 14 days, and get plenty of fresh air and sunshine. She was put on Syr. Ferri. Iod.

She was admitted to the Ward on 29 -8 -32, she looked much better, her liver was still about 1½" inches below the costal margin.

She was given bi-weekly injections of 1c.c. of Bismogenol and Ferri et Quin.Cit. by the mouth. A month later small doses of NK were given with Glucose intra-venously.

Up to 19 -12 -32 she received 1.5 gms. NK and 16 c.c's Bismogenol. She appeared to be very fit and had put on one stone in weight. On this date she developed a slight jaundice. Her arsenic injections were stopped and the Bismuth continued.

The jaundice had not cleared up by 10 -1 -33 so she was transferred back to the medical ward to have hepatic function tests performed. The report was as follows: Van den Berg Direct reaction positive - biphasic Laevulose Tolerance Test - blood sugar curve raised. These showed there was some degree of hepatic insufficiency associated with the enlarged

liver which had not varied in size.

Her blood Wassermann Reaction was still strongly positive. She was discharged from the Medical Ward on 27 -1 -33 and given Hydrary with cum and told to report fortnightly for Bismuth injections.

She reported on four occasions. She was admitted to the Medical Ward as an emergency case and died on 3 -6 -33 from a severe gastric haemorrhage.

Discussion.

This case was diagnosed as one of congenital syphilis in the Medical Ward in the first instance.

Although epistaxis is a known sign in Banti's Disease the blood picture was not typical of this condition in that there was not a definite lymphocytosis.

It is difficult to see why two diseases were diagnosed to explain the symptoms and signs when one would cover them all. The blood picture could readily occur in syphilis as Piney [48] states that "it is commonly admitted that severe anaemia may occur as the result of wide spread syphilitic affection of the liver."

It seems that the enlargement of the spleen was the misleading factor in this case but it must be remembered that any degree of enlargement of the spleen may be encountered in syphilis of the liver. Sections of the spleen were not suggestive of Banti's Disease.

A striking fact which seemed to be overlooked was

the statement made in the Medical Ward that Potassium Iodide reduced the size of the spleen quite considerably. The patient improved under antisyphilitic treatment for in 9 months she put on 2 stones in weight.

Post-mortem the patient was found to have died from haemorrhage from varicose veins at the oesophageal end of the stomach. These were due to portal obstruction from the diffuse fibrotic condition of the liver.

The jaundice which occurred during treatment had probably the same causal mechanism.

Whether the portal obstruction was due to the natural contraction of the fibrous tissue in the liver or whether it was accelerated by antisyphilitic treatment is difficult to say.

One thing seems certain that the patient suffered from the Chronic Interstitial Pericellular Cirrhosis of Heredo-syphilis as this was clearly suggested in the post-mortem report. We may therefore assume that the Splenic condition and the blood picture were also caused by syphilis.

B8857 aet 14 yrs. May 1931.

Admitted to City Hospital May 1931 as T. B. of the outer end of right clavicle. X-ray was suggestive of gumma and Wassermann Reaction was positive.

Swelling over right clavicle had been present for 13 months and had broken down a few weeks prior to admission. It had not yielded to treatment in Leith Hospital where presumed to be Tuberculous in origin.

He was found to have an enlarged liver three finger breadths below costal margin and the Spleen also was greatly enlarged.

He had a complete examination done but no abnormality could be detected in the red or white counts or in the fragility test, bleeding time or coagulation time. The blood film looked normal.

His facies were suggestive, he had slight malar flattening. There were rhagades at the angles of his mouth. His teeth were septic, but not typical of Congenital Syphilis.

Between May and October 1931 in the Edinburgh City Hospital he received:

As. 2.4 Gms

Bi. 1.6 Gms.

He was transferred to Ward 5A on the 27th November 1931.

Liver three finger-breadths below costal margin and Spleen a hand breadth below costal margin.
X-ray showed apparent thickening of upper end of diaphysis of right humerous.
Wassermann Reaction was positive.

His blood count was repeated and found to be 4.3 Million R.B.C's, his Colour Index 1.0.

W.B.C's. 4,200 and differential count. Normal.

He was started on a course of NK and Bis. and transferred to Pilton Hospital on 24th December 1932 where his treatment was continued but Bi. had to be used cautiously because of blue lines on gums.

While in Pilton he complained of pain in the Rt. Iliac fossa and on examination he was found to have friction of both bases.

Splenic Puncture was performed in Pilton but no Gaucher cells were found.

He received in all between 27 : 11 : 31 and 3 : 3 : 32 As. 2.3 Gms. and Bis. .6 Gms.

There was no appreciable difference in the size of Liver or Spleen.

Transferred back to Ward 5A as an Out-patient

Between 14 : 3 : 32 and 13 : 8 : 32 he received 21 c.c's. Cardyl.

24: 9 : 32 Wassermann Reaction positive. (strongly)

8 :10 : 32 Started course of .15 NK and 1 c.c. Cardyl alternately weekly. But did not report from 26 : 11: 32 till 20 : 1 : 33 when he came to report that he had been in bed for three weeks with influenza.

He looked very anaemic. Received 20 c.c. Gluc. .1 NK.

27 : 1 : 33 Patient reported with oedema of both ankles and marked ascites.

Liver and Spleen still as much enlarged.

Given Novasurol ½ c.c. on two occasions and passed 25 ozs. and 20 ozs.

29 : 1 : 33. Transferred to Ward 22. Received no antisyphilitic treatment. Had abdominal paracentesis and general treatment and improved greatly.

4 : 4 : 33. Reported having left Ward 22, two weeks ago, looking well. No ascites or oedema.

Wassermann Reaction positive.(strongly)

Started on course of Bi. but defaulted 19 : 5 ;33.

Reported back 5 : 9 : 33. Saying that he had haematemesis and melaena.

He was very anaemic and looked desperately ill. He was transferred to Ward 22 where it was found necessary to give him a transfusion, his blood count being under two million Reds.

He recovered sufficiently to be up and about in Ward 22. His Liver was two inches below the right costal margin and Spleen four inches below costal margin.

There was practically no difference in the size of his Liver and Spleen as the result of treatment. He again defaulted.

Discussion.

It was found that he was one of a family of congenital syphilitics and that he had attended Ward 20 in 1922 suffering from Interstitial Keratitis.

He received at that time 1.5 Gms of "914" and his mother ceased to bring him for treatment

The diagnosis of a Chronic Interstitial

Pericellular Cirrhosis of Hirèdo-syphilis is the obvious diagnosis in this case.

His case has been included despite the fact that it is not a case of acquired Syphilis because it illustrates the dangers which arise in treatment of such chronic cases.

This child came under my care in the City Hospital and fired by enthusiasm at finding a strongly positive Wassermann Reaction, I started the patient off on dual therapy.

When later I was working in the Venereal Diseases Department I met the patient again and saw the error I had made.

He shows very clearly what is termed the therapeutic paradox. The arsenicals and bismuth administered with more enthusiasm than knowledge most certainly helped to eradicate the syphilitic processes in the liver and spleen but resulted in the contraction of the resultant fibrous tissue. This led to the interference with the portal circulation and the ascites and abdominal pain which the patient experienced.

The profound anaemia which developed was probably due to the toxic action of the arsenic on the bone marrow.

The fact that these untoward results were at once alleviated on cessation of anti-specific treatment bears out the contention that they were the result of the treatment and not the disease.

It was obvious that the child needed treatment when he had devoloped a gumma of his shoulder ten years

after his Interstitial Keratitis. The infection was was still present and active.

I believe that had the treatment been started rationally by first giving the patient a long course of iodides and then small doses of the intra-muscular arsenical, the therapeutic paradox would not have happened and the child's life would have been made more bearable for him.

DISCUSSION.

A brief discussion has been given on each case laying stress on the main facts which point to the diagnosis in the particular case. The treatment carried out on each case has been given and a note on the progress of each case recorded, thus the response to that particular line of treatment can be assessed. I think that a brief review of the different groups of cases would not be amiss.

1. Early Acute Benign Hepatitis.

This is a very definite clinical entity which is characterised by jaundice and some degree of enlargement of the liver.

The most striking feature of the condition is its almost complete lack of symptoms. There is always bile present in the urine but the stools are not always clay coloured - a fact depending on the amount of biliary obstruction present in the case.

There is usually a history of a primary sore and the jaundice often occurs synchronously with the appearance of the secondary rash if present.

The Wassermann Reaction is strongly positive in practically 100% of cases and is the main pointer to the condition. Once the diagnosis is made the treatment should be instituted at once and the rapid response to treatment is very striking.

2. Syphilitic Destructive Hepatitis.

This is probably the most difficult type of syphilitic involvement of the liver to diagnose.

Its very close resemblance to Acute Yellow Atrophy of the liver of different aetiological origin gives the physician in charge of the case a very difficult task to come to a decision on the case.

The fact that the treatment necessary in the syphilitic case is so vastly different from that in other cases does not in any way lighten his responsibility. The two points which help to make the diagnosis easier are the history of syphilis and a positive Wassermann Reaction.

It must be remembered that this condition may be the first indication that the liver is the seat of syphilitic infection. It may come on in the early type of liver affection or may be the ultimate termination of a long standing liver involvement. If the condition arises in a patient receiving treatment for syphilis the possibilities of its being the result of treatment by a certain drug must be considered or else it may be a Herxheimer manifestation.

In either case it is better to change to another drug to be on the safe side. It is a desperate condition and desperate measures are called for. Although the prognosis is extremely bad, patients with all signs of liver atrophy have recovered and therefore once the diagnosis is arrived at it is the duty of the physician in charge to administer treatment and risk untoward results.

3. Chronic Hepatitis of Latency.

This chronic enlargement of the liver is usually found in the course of a routine examination. All

the patient may complain of is a feeling of weight in the abdomen. Despite its symptomless nature it must be borne in mind that it may give rise to trouble at a later date either by causing partial obstruction or an acute atrophy may supervene.

There is often a concomitant splenic enlargement with no symptoms. The Wassermann Reaction is positive in a large proportion of these cases.

It calls for treatment which must be rational for this type of disease which is characterised by a laying down of fibrous tissue.

The best results are obtained when the patient is given a course of iodides prior to the administration of the arsenical drugs.

Much good can be done in these cases but it is often difficult to change the Wassermann Reaction. This is not surprising however when it is recalled that, in many cases of apparently uncomplicated syphilis in which the ordinary courses of treatment fail to change the Wassermann Reaction, a visceral focus of infection is found on more careful examination.

It is interesting to note that in one case good results were obtained in the treatment of the liver on administrating a pentavalent arsenical Tryparsamide which was given for the patient's more pressing complaint - a central nervous system involvement.

4. Diffuse and Gummatous Hepatitis.

These later syphilitic liver conditions are

remarkable for the variety of symptoms which they cause. Syphilis is the great imitator and certainly in the liver it can give collections of symptoms which may simulate any disease of the liver or gall-bladder and some of the blood dyscrasias.

This difficulty in diagnosis has been dealt with more fully in the first section of the thesis and I do not wish to have any unnecessary repetition.

The cases described have shown examples simulating gastric ulcer, malignant disease of the liver and Banti's disease and the lines on which to go in diagnosis have been brought out in the separate discussions on the cases. Of the main aids to diagnosis, or at least to the suggested diagnosis, the Wassermann Reaction is the most helpful. It is positive in anything up to 90% of cases. The history of infection with syphilis some years previously is also useful but can only be obtained in about 50% of cases and therefore does not rank nearly so highly as the Wassermann Reaction as a help in diagnosis.

Of course all the information which can be obtained from the patient as to past history should be obtained and stress laid upon it.

The treatment should be started with iodides as in the latent cases and arsenic given in about 4 - 6 weeks.

A very careful watch should be kept for signs of intolerance to treatment and care should be taken not to precipitate a therapeutic paradox - making the patient's life less bearable as a result of treatment

than it was with the original condition.

The reading of the Wassermann Reaction is difficult to change in these conditions also - but it must be remembered that we are treating a patient and not a Wassermann Reaction. After all if we have made life more pleasant for the patient and lengthened his life the fact that we cannot change his Wasserman Reaction is of small moment.

The prognosis is better in proportion to the preponderance of gummatous lesion over the interstitial fibrosis and although we cannot hope to cure many of these cases we can, with carefully given treatment, affect improvement in practically every case. The bug-bear of this group is the therapeutic paradox and we must guard against it and suspend treatment at once if we suspect it, otherwise disastrous results may follow.

CONCLUSIONS.

1. That syphilis of the liver occurs in a small proportion of cases of syphilis and may develop at any time from the early secondary stage of the disease.

2. That there are various types of liver involvement giving different pathological pictures and demanding different lines of treatment.

3. That syphilis of the liver can give rise to symptoms suggesting almost every other condition of the liver and gall-bladder and

4. That the only definite diagnostic test in Hepatic Syphilis is the Therapeutic test but other aids to diagnosis are:

   a) The finding of a strongly positive Wassermann indicating that the patient is suffering from syphilis. A negative Wassermann Reaction does not mean that the patient has not syphilis;

   b) The history of the patient having been infected with syphilis at some earlier date;

   c) The finding of a healed scar of the primary sore or in the earlier cases the primary sore still present, or the presence of a secondary rash;

   d) Evidence of syphilis of some other region of the body such as the central nervous system or cardio-vascular system.

5. That practically all cases are improved by being given the appropriate treatment indicated in the first part of the thesis, and that the early benign type is apparently cured.

6. That liver efficiency tests only indicate the amount of damage to the organ and do not help in differentiating between syphilis and other pathological conditions of the liver.

From the diversity of symptoms given and the variability of the signs elicited in syphilis of the liver, this condition should be excluded in all pathological processes in the liver.

As the liver is affected in such a definite number of cases, involvement of the liver should be looked for carefully in every patient suffering from syphilis. The finding of it early would, if properly treated save a lot of ill-health occuring in syphilitic patients in later years.

REFERENCES.

1. Modern Clinical Syphilology. 1927. p. 768.
2. Syphilis. 1928 p. 199.
3. Syphilis 1920 p. 314.
4. De Morbo Gallico, Patavii 1564 p. 9.
5. De Morbis Venereis, Paris 1736 p. 319.
6. Treatise on Venereal Disease, Philadelphia 1791 p. 303.
7. Modern Clinical Syphilology 1927 p. 769.
8. Mem. Soc. Biolog. 1853 p. 235.
9. München med. Wchnschr. 1897 No. 27.
10. Syphilis Sydenhan Soc. Lib. 182.
11. Berl. Klin. Wchnschr. 1894 p. 904.
12. Diseases of the Liver, Philadelphia 1905 p. 348.
13. Diseases of the Liver, Pancreas and Supra renal glands. Mothnagel's Encyc. of Pratical Med. American Ed. p. 487.
14. Syphilis 1920 p. 316.
15. Modern Clinical Syphilology 1927 p. 794.
16. Berl. Klin. Wchnschr. 1908 lxv 905.
17. Syphilis 1920 p. 316.
18. Modern Clinical Syphilology 1927 p. 770.
19. Biochem. Ztschr. 1909 xxii 279.
20. Boston Med. and Surg. Jur. 1908 p. 510.
21. Primary Syphilitic Icterns. Paris Med. 1920 p. 141
22. The Diagnosis and Treatment of V. D. 1931 p. 154.
23. Icterus parvus Syphiliticus, Jour. Am. Med. Assn. 1917 lxviii 1311.
24. Modern Clinical Syphilology 1927 p. 768.
25. Modern Clinical Syphilology 1927 p. 794.

26.	Syphilis.	1928	p.	202.
27.	Syphilis of the Liver. Arch of Syph. and Derm	1920	1	139.
28.	Modern Clinical Syphilology	1927		771
29.	Power and Murphy's System of Syph.	1908	iii	42.
30.	New York Medical Jour.	1902	p.	101.
31.	Jour. Am. Med. Assn.	1916	lxvi	1457.
32.	Diseases of the Liver, New Yprk.	1905		
33.	The Diagnosis and Treatment of V. D.	1931	p.	154.
34.	Jour. Am. Med. Assn.	1916	lxvii	1458.
35.	Power and Murphy's System of Syph. Lon.	1908	iii	59.
36.	Mitt a. d. Grenz gets. d. Med. u. Chir.	1904	xiv	781.
37.	Modern Clinical Syphilology.	1927	p.	782.
38.	Lancet. London.	1899	1	301.
39.	Am. Jour. Med. Sc.,	1915		512.
40.	Brit. Med. Jour.	1896.		1445.
41.	Power and Murphy's System of Syphilis.	1908	iii	59.
42	Modern Clinical Syphilogy	1927		780.
43.	Presse Med.	1896		505.
44.	Modern Clinical Syphilology	1927		781.
45.	Am. Jour. Med. Sc.	1910	p.	527.
46.	Syphilis	1920	p.	319.
47.	Modern Clinical Syphilogy.	1927	p.	797.
48.	Diseases of the blood.	1928	p.	154.